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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/461,580	12/15/1999	LEONARD GUARENTE	0050.161800	3988

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225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER

ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 09/05/2003

33

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

## Office Action Summary

Application N .

09/461,580

Applicant(s)

GUARENTE ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2002 and 22 May 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11, 21, 25-61 and 68-168 is/are pending in the application.
- 4a) Of the above claim(s) 28-61 and 68-168 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 21 and 25-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-11, 21, 25-61 and 68-168 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

The amendments and responses filed on 4-9-2002 and 5-22-03 are acknowledged. With regard to the amendment filed on 4-9-2002, claims 1-2, 8, 10-11, 15-16, 21-22 and 25-26 have been amended; claims 62-67 have been added and claim 24 has been canceled. With regard to the amendment filed on 5-22-2003, claims 11 and 21 have been amended; claims 12-20, 22-24 and 62-67 have been canceled; and claims 68-168 have been added.

Newly submitted claims 68-168 are deemed to be directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicant has failed to identify which claims read on the elected invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28-61 and 68-168 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-11, 21 and 25-27 are currently under examination.

### ***Drawings***

The drawings were received on 4-21-2003. These drawings are acceptable.

### ***Claim Rejections Withdrawn***

The rejection of claims 11-20 and 22-24 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn. The amendment of claim 11 and the cancellation of claims 12-20 and 22-24 has rendered the rejection moot.

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The rejection of claims 11, 21 and 24 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “NAD-dependent acetylation status” is withdrawn. The amendment to claim 11 and 21 and the cancellation of claim 24 have rendered the rejection moot.

The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “the histone protein” is withdrawn in light of the amendment thereto.

The rejection of claims 6 and 14 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “removal of an acetyl group” is withdrawn. Applicant’s arguments have been fully considered and deemed persuasive.

The rejection of claims 8, 10, 15, 22, and 26 under 35 U.S.C. 112, second paragraph, for reciting improper Markush language is withdrawn in light of the amendment to claims 8, 10 and 26 and the cancellation of claims 15 and 22.

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “NAD compound” is withdrawn in light of the amendment thereto.

The rejection of claims 6 and 14 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “producing a combination” is withdrawn. Applicant’s arguments with regard to claim 6 has been fully considered and deemed persuasive. Cancellation of claim 14 has rendered the rejection moot.

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The rejection of claims 11 and 21 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “producing a combination” is withdrawn. Applicant’s arguments have been fully considered and deemed persuasive.

The rejection of claims 11 and 21 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “detecting the NAD-dependent status” is withdrawn in light of the amendment thereto.

The rejection of claims 12 and 13 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “activity of the Sir2 protein” is withdrawn. Cancellation of said claims has rendered the rejection moot.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of incomprehensible language is withdrawn. Cancellation of said claim has rendered the rejection moot.

### ***Claim Rejections Maintained***

#### ***35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-10, 21 and 25-27 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reasons of record. The claim(s) contains subject matter that was not described in the specification in such a way as to

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enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

**Applicant argues:**

1. Applicant has defined acetylation status and NAD-dependent acetylation status throughout the specification.
2. Acetylation status is defined as being either the acetylation or deacetylation of a substrate.
3. The specification provides guidance on how to alter acetylation status and how to determine acetylation status. Acetylation status of a histone peptide is altered by Sir2.
4. Acetylation status of a protein can be determined using methods known to one of skill in the art such as electron-spray or MALDI.
5. The specification provides guidance as to the role of Sir2 and histone proteins in the claimed methods. Said methods are drawn to methods of altering the acetylation status of at least one amino acid residue in a protein by altering the activity of Sir2.

Applicant's arguments have been fully considered and deemed non-persuasive.

The specification, as argued by Applicant, defines "acetylation status" as the process of acetylating or deacetylating a substrate. It is unclear how a "status" can be defined by a process. Moreover, Applicant asserts on page 8 of his argument that the specification teaches that Sir2 alters (i.e. either acetylates or deacetylates) histone peptides but then asserts that the instant invention is drawn to methods of altering the acetylation status of at least one amino acid residue in a protein by altering the activity of Sir2. Based on Applicant's disclosure and arguments Sir2 both acetylates and deacetylates proteins. The specification gives no guidance on how one of

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skill in the art would determine whether a given test compound causes the acetylation or the deacetylation of a protein when that is the disclosed activity of Sir2 and Sir2 is always present?

With regard to claim 21 the specification is silent on how the deacetylation of a given substrate in the presence of a given test compound would indicate the ability of said compound to increase the life span of a cell.

Therefore, due to the lack of guidance in the specification and the lack of working examples, one of skill in the art would not be able to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “acetylation status” is maintained for reasons of record. Applicant has argued that said term is defined in the specification as being either the acetylation or deacetylation of a substrate. It is still unclear how a “status” can be defined in terms of a chemical process.

The rejection of claims 1, 6, 11, 21 and 25 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “NAD-dependent acetylation status” is maintained for reasons of record. Applicant has argued that said term is defined in the specification as being either the acetylation or deacetylation of a substrate said process requiring the presence of NAD. It is still unclear how a “status” can be defined in terms of a chemical process.

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Claims 1 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term “alter(ing) the activity of a Sir2 protein” for the reasons set forth previously in the rejection of claim 1. It is unclear what “activity” is being altered. Applicant has argued that the specification discloses that Sir2 has deacetylase activity and hence said the aforementioned term is definite. However, since the specification describes multiple activities for Sir2 (see page 36 of the specification for example), it is unclear to which altered “activity” Applicant is referring.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being vague and indefinite for lacking positive active steps is maintained for reasons of record. The amendment to said claim is insufficient to overcome the rejection. As stated previously, method claims should contain all the steps necessary for carrying out the invention. The amended claim merely adds the limitation that said method comprises the step of altering the activity of a Sir2 protein. There is no correlation between that step and the goal stated in the preamble of the claim.

The rejection of claim 21 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite is maintained since it is still unclear how a change in the acetylation status of a protein correlates to an alteration in the lifespan of a cell.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.



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Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: correlating the deacetylation of said substrate to a Sir2 activity (i.e. determining whether the deacetylation of the substrate is due to the Sir2 protein or the test agent).

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: means of measuring the lifespan of a given cell, determining whether said lifespan has been altered and correlating a given alteration in lifespan to the administration of a given agent.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991.

The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Robert A. Zeman  
September 3, 2003

  
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